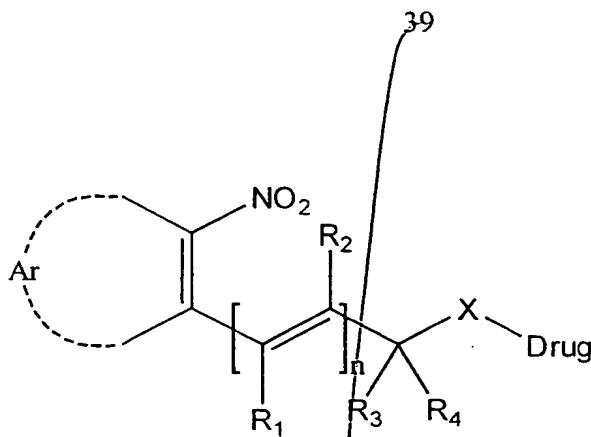


CLAIMS

1. A bioreductive conjugate comprising a bioreductive moiety with at least one therapeutic agent linked thereto and physiologically acceptable derivatives thereof wherein the bioreductive moiety incorporates an aromatic ring substituted with a nitro group and the conjugate is such that bioreduction of the nitro group causes release of the therapeutic agent by a through bond elimination and the residue of the bioreductive moiety to undergo an intramolecular cyclisation reaction in which the nitrogen of the original nitro group provides an atom of the thus formed ring.
2. A conjugate as claimed in claim 1 wherein the bioreductive moiety is non-cytotoxic.
3. A conjugate as claimed in claim 1 or 2 wherein the formation of the ring occurs as a result of a self-alkylation reaction.
4. A conjugate as claimed in any one of claims 1 to 3 wherein the residue of the therapeutic agent to be released on bioreduction is bonded to the aromatic ring *via* a side chain attached to an atom of the aromatic ring adjacent to that to which the nitro group is bonded.
5. A conjugate as claimed in any one of claims 1 to 4 wherein the drug moiety to be released on bioreduction is bonded to the aromatic *via* a side chain incorporating one or more double bonds which are located in the side chain between said moiety and the aromatic ring, which is/are conjugated to the aromatic ring, and which is/are displaceable to provide for elimination of moiety and formation of an arrangement of double bonds such that the residue of the bioreductive moiety is capable of undergoing the intramolecular cyclisation reaction.
6. A conjugate as claimed in claim 5 which is of the general formula (I)



in which

the dashed lines represent completion of a substituted or unsubstituted aromatic ring system;

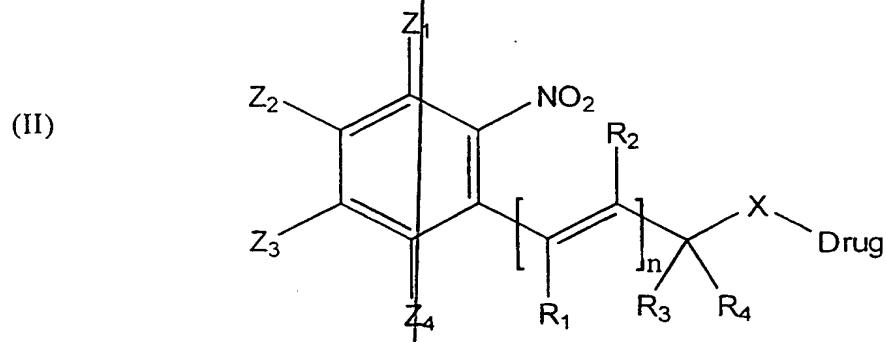
Drug is a therapeutic agent;

X is a linker (which may be part of the drug) and may for example be O, -NH, S, an amide, alcohol, phenol, carboxylic acid (carboxylate), carbonate, phosphate, sulphate or sulphonate;

R_1 , R_2 , R_3 and R_4 are independently hydrogen, substituted or unsubstituted alkyl (e.g. C_{1-4}), aryl, halide, amine, alkoxy, ether, ester, alcohol, phenol, nitro, amide, thiol, sulphate, phosphate, phosphonate; and

n is 1 to 3.

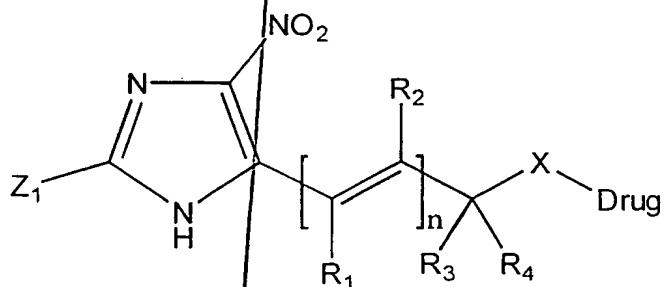
7. A conjugate as claimed in claim 6 which is of the general formula (II)



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8. A conjugate as claimed in claim 6 which is of the general formula (III)

(III)

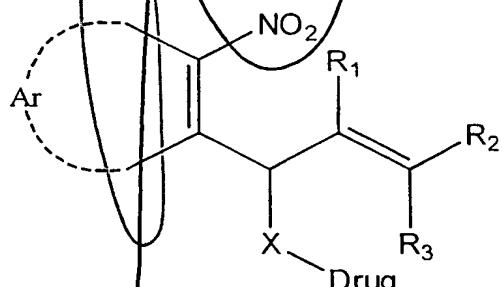


9. A conjugate as claimed in any of claims 6 to 8 wherein n=1.

10. A conjugate as claimed in any one of claims 1 to 5 wherein the drug moiety to be released on bioreduction is bonded to the carbon atom adjacent to the aromatic ring of a side chain bonded to that ring and that carbon atom is bonded to an olefinic double bond of the side chain.

11. A conjugate as claimed in claim 10 which is of the formula (IV)

(IV)



in which

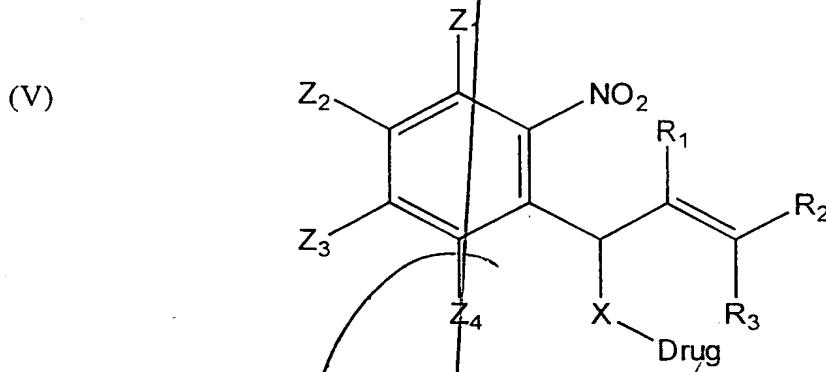
Drug and X are as defined above;

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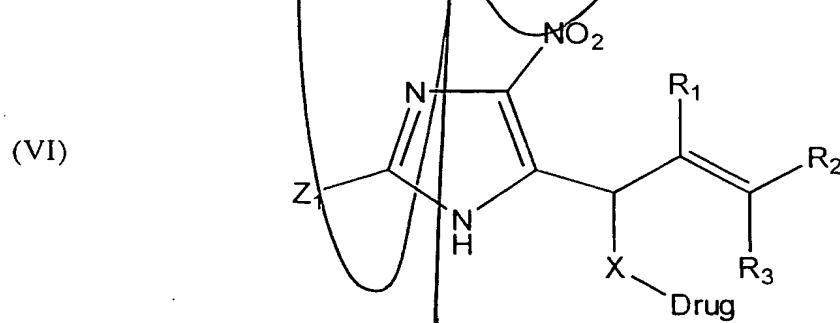
the dashed lines represent completion of a substituted or unsubstituted aromatic ring; and

R_1 , R_2 and R_3 are independently hydrogen, substituted or unsubstituted alkyl (e.g. C_{1-4}), aryl, halide, amine, alkoxy, ether, ester, alcohol, phenol, nitro, amide, thiol, sulphate, phosphate, phosphonate.

12. A conjugate as claimed in claim 11 which is of the formula (V)



13. A conjugate as claimed in claim 11 which is of the formula (VI)



14. A conjugate as claimed in any one of claims 1 to 13 wherein the therapeutic agent is an anti-infective, such as an antibiotic or antiviral agents, analgesic, anaesthetic, anti-inflammatory or anti-neoplastic agent.

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15. A therapeutic composition comprising a bioreductive conjugate as claimed in any one of claims 1 to 14 in conjunction with a therapeutically acceptable carrier.
16. The use of a bioreductive conjugate as claimed in ~~any one of claims 1 to 15~~ for the manufacture of a medicament for therapeutic treatment.
17. The use as claimed in claim 16 wherein the therapeutic treatment is for the treatment of a condition associated with hypoxia and/or ischemia.
18. The use as claimed in claim 16 ~~or 17~~ wherein the medicament is for the treatment of an inflammatory condition, diabetes, atherosclerosis, stroke, sepsis, Alzheimer's disease and other neurological diseases, cancer, kidney disease, digestive diseases, liver disease, chronic periodontitis and ischemia following tissue transplantation.
19. The use as claimed in the claim 18 when the medicament is for the treatment of rheumatoid arthritis or other arthritic condition such as oesteoarthritis.
20. The use as claimed in claim 18 or 19 wherein the medicament is for the treatment of an inflammatory condition of soft tissue.
21. The use as claimed in claim 19 or 20 wherein the medicament is for the treatment of a gastrointestinal disorder, for example, Crohn's disease.
22. The use as claimed in claim 20 or 21 wherein the medicament is for use in the healing of wounds (acute and chronic), and the treatment of fibrotic disorders, ulcerative colitis, inflammatory bowel disease, epilepsy, cardiovascular reperfusion injury, cerebral reperfusion injury, hypertension, cystic fibrosis, psoriasis, para-psoriasis, peptic ulcers, gastric ulcers, duodenal ulcers, diabetic ulcers, dementia, oncology and AIDS.